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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/676,734	09/29/2000	Charles Joel Arntzen	P00245US D	1914

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/676,734	ARNTZEN ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-75,83,84 and 98-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-75,83,84 and 98-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on September 17, 2004 has been entered.

Claims 73, 84, 100, 101 are currently amended.

Claims 1-72, 76-82 and 85-97 are cancelled.

Claims 102-104 are newly added.

Claims 73-75, 83-84 and 98-104 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claim 73-75, 83-84 and 98-101 remain rejected, and claims 102-104 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the transgenic plants expressing the specific animal viral antigens at the levels set forth in Applicant's working examples, does not reasonably provide enablement for expressing in all plants recombinant viral antigen proteins obtained from all animal viruses. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed March 17, 2004.

Applicant's arguments filed September 17, 2004, have been fully considered but they are not persuasive.

With respect to claims 83, 84, 73-75, and 98-101, Applicant submits that the specification is enabling for achieving the levels of expression necessary to elicit an immune response in an animal upon consumption as exemplified in the examples and the detailed teaching of the specification. Applicant further disagrees with the Examiner's prior assertions of unpredictability, and Applicant points in particular to the guidance offered in MPEP Patent Office Rules and Practice § 2164.02 for assessing whether working examples are sufficient to support the enablement of a claimed genus. Applicant maintains that the instant specification clearly has representative, enabling examples in the hepatitis B surface antigen and the TGEV S protein. Applicant additionally points out that a list of candidate antigens from various sources is provided in the specification. (reply pages 5-6).

The Examiner maintains that the disclosure of transgenic plants that express only two recombinant animal viral antigen proteins (recombinant transmissible gastroenteritis virus (TGEV) S-protein and recombinant hepatitis B surface antigen (HbsAg) protein) does not provide sufficient guidance for one skilled in the art to practice the full scope of the claimed invention without undue experimentation, which broadly encompasses transgenic plants comprising nucleotide constructs encoding any unspecified recombinant animal viral antigen protein operably linked to any unspecified promoter that preferentially targets expression to any unspecified tissue of any unspecified plant that is edible by any unspecified organism and any unspecified 5' nontranslated leader sequence wherein said recombinant animal viral antigen protein is expressed at a level sufficient to induce an immune response upon oral administration of said plant to an animal.

With respect to the guidance offered in MPEP Patent Office Rules and Practice § 2164.02, the Examiner maintains that adequate reasons were advanced to establish that a person skilled in the art could not use the genus as a whole without undue experimentation. As discussed previously at pages 3-4 of the office action mailed March 17, 2004 and pages 5-6 of the office action mailed August 13, 2003, the level of expression of different recombinant proteins in transgenic plants is affected by multiple variables, such as the type of promoter used and the stability of expressed mRNA and protein molecules, and is thus unpredictable. The expression of only two different recombinant animal viral antigen proteins at the desired levels in transgenic plants as exemplified in the instant application does not provide sufficient guidance with respect to how one may express a multitude of structurally and functionally distinct animal viral antigen proteins at the desired levels.

In this regard the disclosure of a list of candidate antigens from various sources provided in the specification does not provide sufficient guidance for one skilled in the art to practice the full scope of the claimed invention without undue experimentation because expression in a plant of other candidate antigens at a level sufficient to induce an immune response upon oral administration of said plant to an animal or at a level of at least 43 ng/mg or higher of total soluble protein would require further guidance with respect to how to achieve such levels of expression for each type of candidate antigen.

Applicant further maintains that for one skilled in the pertinent art, i.e. transgenic plant production, the claimed invention can be practiced in the manner disclosed without undue experimentation, since the various factors contributing to the unpredictability

raised by the Examiner as affecting the expression levels of recombinant proteins in transgenic plants were known variables to plant molecular biologists at the time of filing of this application, and these factors were routinely taken into account in an experimental design for transgenic plant production of recombinant proteins. Applicant also maintains that it is also a known fact that for transgenic plant production of recombinant proteins, and accordingly it is always necessary to generate a large population of transgenic plants from which a high producer of the recombinant protein may be selected, and this selection process inevitably involves the working of the various factors raised by the Examiner. Applicant maintains that it therefore cannot be said that the variables set forth by the Examiner would make the instant claims unpredictable or require undue experimentation to practice. (reply pages 6-7)

The Examiner disagrees with Applicant's assertion that one skilled in the art could practice the claimed invention without undue experimentation because the various factors contributing to the unpredictability raised by the Examiner as affecting the expression levels of recombinant proteins in transgenic plants were known variables to plant molecular biologists at the time of filing of this application. The general knowledge possessed by those skilled in the art regarding factors such as the type of promoter used and the stability of expressed mRNA and protein molecules contributing to the unpredictability of the level of expression of recombinants proteins in transgenic plants does not allow those skilled in the art to practice the claimed invention without undue experimentation, because one skilled in the art would still require specific guidance with respect to how to control these variables for each particular recombinant animal viral antigen protein and each particular expression system used in order to express the

particular recombinant animal viral antigen protein at a particular level. Absent such guidance one skilled in the art could generate a large population of transgenic plants and still be unable to select a plant that produces the recombinant animal viral antigen protein at the claimed levels, because even the highest producer of the recombinant protein selected might not produce the recombinant protein at a level sufficient to induce an immune response upon oral administration of said plant to an animal, or at a level of at least 43 ng/mg or higher of total soluble protein.

Applicant also directs the Examiner's attention to another successful example of expression in plants of HIV-related proteins (U.S. Patent Application No. 20040040061). Applicant maintains that the production of these HIV related surface protein in plants is carried out in roughly the same manner as those disclosed in the instant specification. Applicant further directs the Examiner's attention to yet another successful example of expression of antigens in plants is shown in U.S. Patent Application 200475441 which shows the successful expression of fish antigens in plants, including avidin and infectious pancreatic necrosis virus VP2 and VP3 using the methods of this invention. (reply page 7)

With respect to U.S. Patent Application 20040040061 (Horn et al., published February 26, 2004), the application does not support the enablement of the full scope of the claimed invention because the HIV-related protein antigens referred to were not expressed in plants using the disclosed methods. The sequences encoding the HIV-related protein antigens expressed by Horn et al. were codon optimized for maize and operably linked to a barley alpha amylase secretion signal coding sequence, a PinII terminator

sequence and a pGNpr4 promoter sequence and expressed in maize plants, whereas the sequence encoding the recombinant transmissible gastroenteritis virus (TGEV) S-protein expressed by Applicant was operably linked to a patatin promoter sequence and a NOS polyadenylation sequence and expressed in potato plants, and the recombinant hepatitis B surface antigen (HbsAg) protein expressed by Applicant was operably linked to a GUS termination sequence, a NOS polyadenylation sequence and a CaMV 35S promoter or a CaMV 35S promoter sequence with a dual transcription enhancer sequence linked to the TEV 5' nontranslated leader sequence, and expressed in tobacco and tomato plants.

With respect to U.S. Patent Application 20040175441 (Bootland et al., published September 9, 2004), the application does not support the enablement of the full scope of the claimed invention because the antigens referred to, avidin (which is not a recombinant animal viral antigen protein as required by the currently rejected claims), and infectious pancreatic necrosis virus VP2 and VP3 proteins, were not expressed in plants using the disclosed methods. The sequences encoding the infectious pancreatic necrosis virus VP2 and VP3 proteins expressed by Bootland et al. were codon optimized for maize, operably linked to a maize codon optimized barley alpha amylase secretion signal coding sequence, a PinII terminator sequence and a pGNpr2 promoter sequence and expressed in maize plants, whereas the sequence encoding the recombinant transmissible gastroenteritis virus (TGEV) S-protein expressed by Applicant was operably linked to a patatin promoter sequence and a NOS polyadenylation sequence and expressed in potato plants, and the recombinant hepatitis B surface antigen (HbsAg) protein expressed by Applicant was operably linked to a GUS termination sequence, a NOS polyadenylation sequence and a CaMV 35S promoter or a CaMV 35S promoter sequence with a dual

transcription enhancer sequence linked to the TEV 5' nontranslated leader sequence, and expressed in tobacco and tomato plants.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 102-104 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 8 of U.S. Patent No. 6,136,320. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are directed to transgenic plants that comprise and express the same type of transgene. Claims 102-104 of the instant application are directed to transgenic plants which express a DNA sequence coding for a surface antigen or antigenic determinant thereof of hepatitis B virus, including a hepatitis B virus surface antigen, or of transmissible gastroenteritis virus, including a transmissible gastroenteritis virus spike protein, whereas claim 8 of U.S. Patent No. 6,136,320 is directed to a plant composition comprising a viral antigen which triggers production of antibodies and which is derived from a hepatitis B virus surface antigen or transmissible gastroenteritis

virus spike protein, and plant material; said antigen being a product produced by the method of expressing said immunogen in a transgenic plant, said plant material being in a form chosen from the group consisting of a whole plant, plant part, or a crude plant extract.

Claims 102-104 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,034,298. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are directed to transgenic plants that comprise and express the same type of transgene. Claims 102-104 of the instant application are directed to transgenic plants which express a DNA sequence coding for a surface antigen or antigenic determinant thereof of transmissible gastroenteritis virus, whereas claims 1-3 of U.S. Patent No. 6,034,298 are directed to a transgenic plant expressing a nucleotide sequence which encodes a recombinant viral antigenic protein, said recombinant protein derived from Transmissible Gastroenteritis virus.

Claims 102-104 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,914,123. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are directed to transgenic plants that comprise and express the same type of transgene. Claims 102-104 of the instant application are directed to transgenic plants which express a DNA sequence coding for a surface antigen or antigenic determinant thereof of hepatitis B virus, including a hepatitis B virus surface

antigen, or of transmissible gastroenteritis virus, including a transmissible gastroenteritis virus spike protein, whereas claims 1-7 of U.S. Patent No. 5,914,123 are directed to a food comprising transgenic plant material capable of being ingested for its nutritional value, said transgenic plant expressing a recombinant immunogen derived from Hepatitis virus, including Hepatitis B surface antigen and a food comprising transgenic plant material capable of being ingested for its nutritional value, said transgenic plant expressing a recombinant immunogen derived from Transmissible Gastroenteritis Virus, including Transmissible Gastroenteritis Virus S.

Claims 102-104 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-14 of U.S. Patent No. 5,484,719. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are directed to transgenic plants that are produced by the methods claimed in U.S. Patent No. 5,484,719. Claims 102-104 of the instant application are directed to transgenic plants which express a DNA sequence coding for a surface antigen or antigenic determinant thereof of hepatitis B virus, including a hepatitis B virus surface antigen, whereas claims 5-14 of U.S. Patent No. 5,484,719 are directed to a method for constructing a transgenic tobacco plant cell comprising: constructing a plasmid vector by operably linking a DNA sequence, said sequence encoding a hepatitis B viral surface antigen protein, to a plant-functional promoter capable of directing the synthesis of said protein in said tobacco plant; and transforming a tobacco plant cell with said plasmid vector, said method further comprising the step of regenerating a transgenic plant from said transgenic plant cell.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Examiner
Art Unit 1638

CC

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